



Clinical trial results:

Phase 3 Study Comparing Daratumumab, Lenalidomide, and Dexamethasone (DRd) vs Lenalidomide and Dexamethasone (Rd) in Subjects With Relapsed or Refractory Multiple Myeloma

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2013-005525-23 |
| Trial protocol | SE GB ES DE BE NL DK PL GR |
| Global end of trial date | 30 September 2021 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 18 November 2023 |
| First version publication date | 18 November 2023 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | 54767414MMY3003 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02076009 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Janssen Research & Development, LLC |
| Sponsor organisation address | 1400 McKean Road, PO Box 776 Spring House, United States, 19477 |
| Public contact | Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 30 September 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 September 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to compare the efficacy of daratumumab when combined with lenalidomide and dexamethasone (DRd) to that of lenalidomide and dexamethasone (Rd), in terms of progression-free survival (PFS) in subjects with relapsed or refractory multiple myeloma.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 16 June 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 18 |
| Country: Number of subjects enrolled | Belgium: 21 |
| Country: Number of subjects enrolled | Canada: 34 |
| Country: Number of subjects enrolled | Germany: 18 |
| Country: Number of subjects enrolled | Denmark: 17 |
| Country: Number of subjects enrolled | Spain: 51 |
| Country: Number of subjects enrolled | France: 58 |
| Country: Number of subjects enrolled | United Kingdom: 51 |
| Country: Number of subjects enrolled | Greece: 19 |
| Country: Number of subjects enrolled | Israel: 39 |
| Country: Number of subjects enrolled | Japan: 36 |
| Country: Number of subjects enrolled | Korea, Republic of: 40 |
| Country: Number of subjects enrolled | Netherlands: 4 |
| Country: Number of subjects enrolled | Poland: 28 |
| Country: Number of subjects enrolled | Russian Federation: 48 |
| Country: Number of subjects enrolled | Sweden: 31 |
| Country: Number of subjects enrolled | Taiwan: 20 |
| Country: Number of subjects enrolled | United States: 36 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 569 |
| EEA total number of subjects | 247 |

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 273 |
| From 65 to 84 years | 292 |
| 85 years and over | 4 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 569 subjects were randomised, of which 564 were treated (283 in the daratumumab, lenalidomide, low-dose dexamethasone [DRd] group and 281 in the lenalidomide, low-dose dexamethasone [Rd] group). None of the subjects completed the study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Lenalidomide, Low-dose Dexamethasone (Rd) |

Arm description:

Subjects received lenalidomide at a dose of 25 milligrams (mg) orally on Day 1 through Day 21 of each 28-day treatment cycle and low-dose dexamethasone at a total dose of 40 mg weekly (or 20 mg weekly for subjects greater than [$>$] 75 years old or with a body mass index less than [$<$] 18.5 kilograms per meter square [kg/m^2]).

| | |
|--|-----------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Low-dose Dexamethasone (Rd) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received low-dose dexamethasone 40 mg weekly (or 20 mg weekly for subjects greater than [$>$] 75 years old or with a body mass index less than [$<$] 18.5 kilograms per meter square [kg/m^2]).

| | |
|--|--------------|
| Investigational medicinal product name | Lenalidomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received lenalidomide 25 milligrams (mg) from Day 1 through Day 21 of each 28-day treatment cycle.

| | |
|------------------|---|
| Arm title | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) |
|------------------|---|

Arm description:

Subjects received daratumumab 16 milligrams per kilogram (mg/kg) as an intravenous (IV) infusion once a week during treatment cycles 1 and 2 (for 8 weeks, each 28-day cycle); every 2 weeks during treatment cycles 3 to 6 (for 16 weeks, each 28-day cycle); once only on Day 1 during treatment cycles 7 onwards (for every 4 weeks). Lenalidomide was administered at a dose of 25 mg orally on Day 1 through Day 21 of each 28-day treatment cycle and low-dose dexamethasone was administered at a total dose of 40 mg weekly (or 20 mg weekly for subjects >75 years old or with a body mass index $< 18.5 \text{ kg}/\text{m}^2$).

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--------------|
| Investigational medicinal product name | Lenalidomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received lenalidomide 25 mg from Day 1 through Day 21 of each 28-day treatment cycle.

| | |
|--|-----------------------|
| Investigational medicinal product name | Daratumumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

Subjects received daratumumab 16 mg/kg once a week during treatment cycles 1 and 2 (for 8 weeks, each 28-day cycle); every 2 weeks during treatment cycles 3 to 6 (for 16 weeks, each 28-day cycle); once only on Day 1 during treatment cycles 7 onwards (for every 4 weeks).

| | |
|--|-----------------------------|
| Investigational medicinal product name | Low-dose Dexamethasone (Rd) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received low-dose dexamethasone 40 mg weekly (or 20 mg weekly for subjects >75 years old or with a body mass index <18.5 kg/m²).

| Number of subjects in period 1 | Lenalidomide, Low-dose Dexamethasone (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) |
|--------------------------------|---|---|
| | | |
| Started | 283 | 286 |
| Treated (Safety population) | 281 | 283 |
| Completed | 0 | 0 |
| Not completed | 283 | 286 |
| Adverse event, serious fatal | 172 | 153 |
| Consent withdrawn by subject | 16 | 12 |
| Physician decision | - | 1 |
| End of data collection | 90 | 118 |
| Lost to follow-up | 4 | 2 |
| Progressive disease | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Lenalidomide, Low-dose Dexamethasone (Rd) |
|-----------------------|---|

Reporting group description:

Subjects received lenalidomide at a dose of 25 milligrams (mg) orally on Day 1 through Day 21 of each 28-day treatment cycle and low-dose dexamethasone at a total dose of 40 mg weekly (or 20 mg weekly for subjects greater than [$>$] 75 years old or with a body mass index less than [$<$] 18.5 kilograms per meter square [kg/m^2]).

| | |
|-----------------------|---|
| Reporting group title | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) |
|-----------------------|---|

Reporting group description:

Subjects received daratumumab 16 milligrams per kilogram (mg/kg) as an intravenous (IV) infusion once a week during treatment cycles 1 and 2 (for 8 weeks, each 28-day cycle); every 2 weeks during treatment cycles 3 to 6 (for 16 weeks, each 28-day cycle); once only on Day 1 during treatment cycles 7 onwards (for every 4 weeks). Lenalidomide was administered at a dose of 25 mg orally on Day 1 through Day 21 of each 28-day treatment cycle and low-dose dexamethasone was administered at a total dose of 40 mg weekly (or 20 mg weekly for subjects >75 years old or with a body mass index $< 18.5 \text{ kg}/\text{m}^2$).

| Reporting group values | Lenalidomide, Low-dose Dexamethasone (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | Total |
|---|---|---|-------|
| Number of subjects | 283 | 286 | 569 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 140 | 133 | 273 |
| From 65 to 84 years | 140 | 152 | 292 |
| 85 years and over | 3 | 1 | 4 |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 64.3 | 64.4 | - |
| standard deviation | ± 8.84 | ± 9.03 | |
| Title for Gender Units: subjects | | | |
| Female | 119 | 113 | 232 |
| Male | 164 | 173 | 337 |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Lenalidomide, Low-dose Dexamethasone (Rd) |
| Reporting group description: Subjects received lenalidomide at a dose of 25 milligrams (mg) orally on Day 1 through Day 21 of each 28-day treatment cycle and low-dose dexamethasone at a total dose of 40 mg weekly (or 20 mg weekly for subjects greater than [$>$] 75 years old or with a body mass index less than [$<$] 18.5 kilograms per meter square [kg/m^2]). | |
| Reporting group title | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) |
| Reporting group description: Subjects received daratumumab 16 milligrams per kilogram (mg/kg) as an intravenous (IV) infusion once a week during treatment cycles 1 and 2 (for 8 weeks, each 28-day cycle); every 2 weeks during treatment cycles 3 to 6 (for 16 weeks, each 28-day cycle); once only on Day 1 during treatment cycles 7 onwards (for every 4 weeks). Lenalidomide was administered at a dose of 25 mg orally on Day 1 through Day 21 of each 28-day treatment cycle and low-dose dexamethasone was administered at a total dose of 40 mg weekly (or 20 mg weekly for subjects >75 years old or with a body mass index $< 18.5 \text{ kg}/\text{m}^2$). | |

Primary: Progression-free Survival (PFS)

| | |
|---|--|
| End point title | Progression-free Survival (PFS) ^[1] |
| End point description: PFS: time from randomisation to progressive disease(PD)/death. PD, any 1 criteria: $\geq 25\%$ increase in serum M-protein level from lowest response value, absolute increase ≥ 0.5 gram per deciliter(g/dL); $\geq 25\%$ increase in 24hours(h) in urinary light chain excretion (urine M-protein) from lowest response value, absolute increase $\geq 200\text{mg}/24\text{h}$; in subjects without measurable serum and urine M-protein levels: $\geq 25\%$ increase in difference between involved and uninvolved free light chain levels from lowest response value and absolute increase $>10 \text{ mg}/\text{dL}$; increase in existing bone lesions/soft tissue plasmacytomas size; development of new bone lesions/soft tissue plasmacytomas; development of hypercalcemia(corrected serum calcium $>11.5\text{mg}/\text{dL}$) attributed to plasma cell proliferative disorder. Intent-to-treat: subjects randomly assigned to DRd or Rd group. 99999: median, upper and lower limit of 95% CI in DRd arm and upper limit of 95% CI in Rd arm not estimable due to short follow-up by subjects. | |
| End point type | Primary |
| End point timeframe: From randomisation to either disease progression or death whichever occurs first (up to 21 months) | |
| Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only descriptive data was planned to be reported for this endpoint. | |

| End point values | Lenalidomide, Low-dose Dexamethasone (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 283 | 286 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 18.43 (13.86 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Disease Progression (TTP)

| | |
|-----------------|-----------------------------------|
| End point title | Time to Disease Progression (TTP) |
|-----------------|-----------------------------------|

End point description:

TTP: time from date of randomization to date of first documented PD. PD, any 1 criteria: $\geq 25\%$ increase in serum M-protein level from lowest response value, absolute increase ≥ 0.5 g/dL; $\geq 25\%$ increase in 24h in urinary light chain excretion (urine M-protein) from lowest response value, absolute increase ≥ 200 mg/24h; in subjects without measurable serum and urine M-protein levels: $\geq 25\%$ increase in difference between involved and uninvolved free light chain (FLC) levels from lowest response value and absolute increase > 10 mg/dL; increase in existing bone lesions/soft tissue plasmacytomas size; development of new bone lesions/soft tissue plasmacytomas; development of hypercalcemia (corrected serum calcium > 11.5 mg/dL) attributed to plasma cell (PC) proliferative disorder. Intent-to-treat: subjects randomly assigned to DRd or Rd group. 99999: median, upper and lower limit of 95% CI in DRd arm and upper limit of 95% CI in Rd arm not estimable due to short follow-up by subjects.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From randomisation to disease progression (up to 21 months)

| End point values | Lenalidomide, Low-dose Dexamethasone (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 283 | 286 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 18.43 (14.78 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved Very Good Partial Response (VGPR) or Better as per International Myeloma Working Group criteria (IMWG)

| | |
|-----------------|--|
| End point title | Percentage of Subjects who Achieved Very Good Partial Response (VGPR) or Better as per International Myeloma Working Group criteria (IMWG) |
|-----------------|--|

End point description:

VGPR or better: Percentage of subjects who achieved VGPR, complete response (CR) and stringent complete response (sCR) as per IMWG. IMWG criteria: Serum and urine M-component detectable by immunofixation but not on electrophoresis or $\geq 90\%$ reduction in serum M-protein plus urine M-protein < 100 mg/24h, if serum and urine M-protein are not measurable, decrease of $> 90\%$ in difference between involved and uninvolved FLC levels is required in place of M-protein criteria. Additionally, $\geq 50\%$ reduction in size of soft tissue plasmacytomas is required at baseline; CR: Negative immunofixation on serum and urine, disappearance of soft tissue plasmacytomas, $< 5\%$ PCs in bone marrow; sCR: CR and normal FLC ratio, absence of clonal PCs by immunohistochemistry, immunofluorescence or 2-4 color flow cytometry. Response-evaluable set: subjects who have confirmed diagnosis of multiple myeloma, measurable disease and must received at least 1 dose of study drug and at least 1 post baseline disease assessment.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From randomisation to disease progression (up to 21 months) | |

| End point values | Lenalidomide, Low-dose Dexamethasone (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 276 | 281 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 44.2 (38.3 to 50.3) | 75.8 (70.4 to 80.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Negative Minimal Residual Disease (MRD)

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Negative Minimal Residual Disease (MRD) |
|-----------------|---|

End point description:

Minimal residual disease was assessed for all subjects who achieved a complete response (CR) or stringent complete response (sCR). CR: Negative immunofixation on the serum and urine, disappearance of any soft tissue plasmacytomas, and <5% PCs in bone marrow; sCR: CR and normal FLC ratio, absence of clonal PCs by immunohistochemistry, immunofluorescence or 2- to 4 color flow cytometry. The MRD negativity rate was defined as the percentage of subjects who had negative MRD assessment at any time point after the first dose of study drugs by evaluation of bone marrow aspirates or whole blood at 10^{-4} , 10^{-5} , 10^{-6} threshold. ITT analysis set included all subjects who were randomly assigned to the DRd or Rd group.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From randomisation to date of first documented evidence of PD (up to 87.5 months) | |

| End point values | Lenalidomide, Low-dose Dexamethasone (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | | |
|---------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 283 | 286 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| MRD negative rate (10^{-4}) | 10.2 | 40.6 | | |
| MRD negative rate (10^{-5}) | 6.7 | 33.2 | | |
| MRD negative rate (10^{-6}) | 1.8 | 13.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate

| | |
|-----------------|-----------------------|
| End point title | Overall Response Rate |
|-----------------|-----------------------|

End point description:

Overall response rate was defined as the percentage of Subjects who achieved a partial response (PR) or better according to the International Myeloma Working Group (IMWG) criteria, during or after study treatment. IMWG criteria for PR: $\geq 50\%$ reduction of serum M-protein and reduction in 24-hour urinary M-protein by $\geq 90\%$ or to < 200 mg/24 hours, if the serum and urine M-protein are not measurable, a decrease of $\geq 50\%$ in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria, in addition to the above criteria, if present at baseline, a $\geq 50\%$ reduction in the size of soft tissue plasmacytomas is also required. Response-evaluable set included subjects who have a confirmed diagnosis of multiple myeloma and measurable disease and must have received at least 1 administration of study treatment and have at least 1 post baseline disease assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From randomisation to disease progression (up to 21 months)

| End point values | Lenalidomide, Low-dose Dexamethasone (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 276 | 281 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 76.4 | 92.9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

| | |
|-----------------|------------------|
| End point title | Time to Response |
|-----------------|------------------|

End point description:

Time to response was defined as the time between the date of randomisation and the first efficacy evaluation that the subject met all criteria for partial response (PR) or better. Response-evaluable set (RES) is defined as subjects who have a confirmed diagnosis of multiple myeloma and measurable disease at baseline or screening visit. In addition, subjects must have received at least 1 administration of study treatment and have at least 1 post baseline disease assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From randomisation up to first documented CR or PR (up to 21 months)

| End point values | Lenalidomide, Low-dose Dexamethason e (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethason e (DRd) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 276 | 281 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 1.3 (1.1 to 1.9) | 1.0 (1.0 to 1.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

| | |
|-----------------|-----------------------|
| End point title | Overall Survival (OS) |
|-----------------|-----------------------|

End point description:

Overall survival was measured from the date of randomisation to the date of the subject's death. ITT analysis set included all subjects who were randomly assigned to the DRd or Rd group. Here 'N' (number of subjects analyzed) signifies number of subjects who were evaluable for this outcome measure.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From randomisation to date of death due to any cause (up to 87.5 months)

| End point values | Lenalidomide, Low-dose Dexamethason e (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethason e (DRd) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 153 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 51.84 (43.99 to 60.02) | 67.58 (53.13 to 80.53) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

| | |
|-----------------|----------------------------|
| End point title | Duration of Response (DOR) |
|-----------------|----------------------------|

End point description:

DOR: time between first documented confirmed response (PR or better) and disease progression/death due to PD, whichever occurs first. PD, any 1 criteria: $\geq 25\%$ increase in serum M-protein level from lowest response value, absolute increase ≥ 0.5 g/dL; $\geq 25\%$ increase in 24h in urinary light chain excretion (urine M-protein) from lowest response value, absolute increase ≥ 200 mg/24h; subjects without measurable serum and urine M-protein levels: $\geq 25\%$ increase in difference between involved and uninvolved FLC levels from lowest response value and absolute increase > 10 mg/dL; increase in size of existing and development of new bone lesions/soft tissue plasmacytomas; development of hypercalcemia (corrected serum calcium > 11.5 mg/dL) attributed to PC proliferative disorder. RES was evaluated. N=subjects who had PR/better response. 99999: median, upper and lower limit of 95% CI in DRd arm and upper limit of 95% CI in Rd arm not estimable due to short follow-up by subjects.

End point type

Secondary

End point timeframe:

From randomisation to the date of first documented evidence of PD (up to 21 months)

| End point values | Lenalidomide, Low-dose Dexamethasone (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 211 | 261 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 17.4 (17.4 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Subsequent Anticancer Treatment**End point title**

Time to Subsequent Anticancer Treatment

End point description:

Time to subsequent anticancer treatment was defined as the time from randomization to the start of subsequent anticancer treatment or death due to progressive disease (PD), whichever occurs first. ITT analysis set included all subjects who were randomly assigned to the DRd or Rd group, and who started subsequent anticancer therapy or died due to progressive disease, whichever occurs first.

End point type

Secondary

End point timeframe:

From randomisation to date of start of subsequent anticancer treatment or death due to PD, whichever occurred first (up to 87.5 months)

| End point values | Lenalidomide, Low-dose Dexamethasone (Rd) | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 212 | 138 | | |
| Units: Months | | | | |

| | | | | |
|----------------------------------|---------------------|---------------------|--|--|
| median (confidence interval 95%) | 23.1 (18.6 to 26.3) | 69.3 (49.7 to 82.8) | | |
|----------------------------------|---------------------|---------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomisation up to 30 days after last dose of study treatment (up to 87.5 months)

Adverse event reporting additional description:

Safety analysis set included all randomised subjects who had at least 1 administration of any study treatment (partial or complete). In arm daratumumab, lenalidomide, low-dose dexamethasone (DRd), 1 subject had death event who was randomised but not treated, therefore, not included in safety analysis set.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) |
|-----------------------|---|

Reporting group description:

Subjects received daratumumab 16 milligrams per kilogram (mg/kg) as an intravenous (IV) infusion once a week during treatment cycles 1 and 2 (for 8 weeks, each 28-day cycle); every 2 weeks during treatment cycles 3 to 6 (for 16 weeks, each 28-day cycle); once only on Day 1 during treatment cycles 7 onwards (for every 4 weeks). Lenalidomide was administered at a dose of 25 mg orally on Day 1 through Day 21 of each 28-day treatment cycle and low-dose dexamethasone was administered at a total dose of 40 mg weekly (or 20 mg weekly for subjects >75 years old or with a body mass index < 18.5 kg/m²).

| | |
|-----------------------|---|
| Reporting group title | Lenalidomide, Low-dose Dexamethasone (Rd) |
|-----------------------|---|

Reporting group description:

Subjects received lenalidomide at a dose of 25 milligrams (mg) orally on Day 1 through Day 21 of each 28-day treatment cycle and low-dose dexamethasone at a total dose of 40 mg weekly (or 20 mg weekly for subjects greater than [$>$] 75 years old or with a body mass index less than [$<$] 18.5 kilograms per meter square [kg/m²]).

| Serious adverse events | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | Lenalidomide, Low-dose Dexamethasone (Rd) | |
|---|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 205 / 283 (72.44%) | 148 / 281 (52.67%) | |
| number of deaths (all causes) | 152 | 175 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma gastric | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute monocytic leukaemia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 1 / 1 | |
| Adenocarcinoma | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenoma benign | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign anorectal neoplasm | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bowen's disease | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clear cell renal cell carcinoma | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal adenocarcinoma | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epstein-Barr virus associated lymphoproliferative disorder | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelodysplastic syndrome | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Plasma cell leukaemia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin cancer | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transitional cell carcinoma | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural mesothelioma | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Aortic aneurysm rupture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolism | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral artery embolism | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hypotension | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery stenosis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic infarction | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous occlusion | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gait disturbance | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hernia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 2 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 3 / 281 (1.07%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 13 / 283 (4.59%) | 5 / 281 (1.78%) | |
| occurrences causally related to treatment / all | 5 / 17 | 4 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 1 | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Sarcoidosis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Social circumstances | | | |
| Loss of personal independence in daily activities | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Reproductive system and breast disorders | | | |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatomegaly | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Obstructive airways disorder | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Asthma | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchospasm | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 283 (1.77%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 4 / 5 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pulmonary calcification | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Respiratory failure | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 12 / 283 (4.24%) | 10 / 281 (3.56%) | |
| occurrences causally related to treatment / all | 11 / 12 | 10 / 10 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depressive symptom | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Influenza B virus test positive | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diagnostic procedure | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urine output decreased | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatic specific antigen increased | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Troponin increased | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|-----------------|-----------------|--|
| Acetabulum fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical vertebral fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Compression fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Concussion | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 4 / 283 (1.41%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle fracture | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Forearm fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Scapula fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Patella fracture | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peroneal nerve injury | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Posterior capsule rupture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound decomposition | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 4 / 281 (1.42%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 5 / 283 (1.77%) | 3 / 281 (1.07%) | |
| occurrences causally related to treatment / all | 2 / 6 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 1 | |
| Cardiac failure | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac failure acute | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 4 / 283 (1.41%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac amyloidosis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery insufficiency | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Left ventricular failure | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Right ventricular failure | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus arrhythmia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systolic dysfunction | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid arteriosclerosis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral arteriosclerosis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorder | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cognitive disorder | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Facial paralysis | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intercostal neuralgia | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 5 / 283 (1.77%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 3 / 8 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Trigeminal nerve disorder | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Bone marrow failure | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 283 (1.77%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 4 / 5 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 13 / 283 (4.59%) | 4 / 281 (1.42%) | |
| occurrences causally related to treatment / all | 13 / 16 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hyperviscosity syndrome | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 5 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sideroblastic anaemia | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombotic thrombocytopenic purpura | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 3 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Visual field defect | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract | | | |
| subjects affected / exposed | 4 / 283 (1.41%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 5 / 5 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Keratitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal detachment | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 8 / 283 (2.83%) | 6 / 281 (2.14%) | |
| occurrences causally related to treatment / all | 6 / 9 | 3 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal vascular malformation haemorrhagic | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticular perforation | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiatus hernia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incarcerated inguinal hernia | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine polyp | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 3 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peptic ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Strangulated umbilical hernia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash papular | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermal cyst | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute kidney injury | | | |
| subjects affected / exposed | 8 / 283 (2.83%) | 11 / 281 (3.91%) | |
| occurrences causally related to treatment / all | 0 / 11 | 5 / 14 | |
| deaths causally related to treatment / all | 0 / 1 | 1 / 3 | |
| Azotaemia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 5 / 281 (1.78%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Urethral haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 6 / 281 (2.14%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone pain | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Flank pain | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal stenosis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spondylolisthesis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertebral foraminal stenosis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spondylitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenovirus infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis infective | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 10 / 283 (3.53%) | 7 / 281 (2.49%) | |
| occurrences causally related to treatment / all | 4 / 12 | 4 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis bacterial | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brucellosis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Candida infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Catheter site infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus chorioretinitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epstein-Barr virus infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epiglottitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocarditis bacterial | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia pyelonephritis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extradural abscess | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| H1N1 influenza | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemophilus infection | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 283 (1.41%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 4 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective spondylitis | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective exacerbation of bronchiectasis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 6 / 281 (2.14%) | |
| occurrences causally related to treatment / all | 2 / 3 | 4 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung abscess | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 14 / 283 (4.95%) | 3 / 281 (1.07%) | |
| occurrences causally related to treatment / all | 9 / 16 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Listeria sepsis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Legionella infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 12 / 283 (4.24%) | 7 / 281 (2.49%) | |
| occurrences causally related to treatment / all | 2 / 14 | 2 / 7 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Intervertebral discitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Keratitis fungal | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis bacterial | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metapneumovirus infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal abscess | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parotitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oral fungal infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 3 / 281 (1.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nocardiosis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 48 / 283 (16.96%) | 32 / 281 (11.39%) | |
| occurrences causally related to treatment / all | 41 / 71 | 16 / 42 | |
| deaths causally related to treatment / all | 2 / 2 | 0 / 3 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Pneumonia haemophilus | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia influenzal | | | |
| subjects affected / exposed | 7 / 283 (2.47%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia klebsiella | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia legionella | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia parainfluenzae viral | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia pseudomonal | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia staphylococcal | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Progressive multifocal leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salmonellosis | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 5 / 283 (1.77%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 1 / 6 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhinovirus infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salmonella bacteraemia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 7 / 283 (2.47%) | 8 / 281 (2.85%) | |
| occurrences causally related to treatment / all | 6 / 9 | 1 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | |
| Septic shock | | | |
| subjects affected / exposed | 4 / 283 (1.41%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 4 / 7 | 0 / 2 | |
| deaths causally related to treatment / all | 2 / 4 | 0 / 1 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue infection | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tuberculosis | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 7 / 281 (2.49%) | |
| occurrences causally related to treatment / all | 3 / 4 | 5 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 7 / 283 (2.47%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 1 / 10 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine abscess | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varicella zoster virus infection | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular device infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 283 (0.00%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 2 / 283 (0.71%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gout | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 283 (0.00%) | 2 / 281 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 3 / 283 (1.06%) | 1 / 281 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 1 / 283 (0.35%) | 0 / 281 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Daratumumab, Lenalidomide, Low-dose Dexamethasone (DRd) | Lenalidomide, Low-dose Dexamethasone (Rd) | |
|---|---|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 278 / 283 (98.23%) | 268 / 281 (95.37%) | |
| Vascular disorders | | | |
| Hypotension | | | |

| | | | |
|--|--------------------|-------------------|--|
| subjects affected / exposed | 26 / 283 (9.19%) | 9 / 281 (3.20%) | |
| occurrences (all) | 32 | 10 | |
| Hypertension | | | |
| subjects affected / exposed | 31 / 283 (10.95%) | 22 / 281 (7.83%) | |
| occurrences (all) | 41 | 24 | |
| Haematoma | | | |
| subjects affected / exposed | 15 / 283 (5.30%) | 6 / 281 (2.14%) | |
| occurrences (all) | 15 | 7 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 59 / 283 (20.85%) | 47 / 281 (16.73%) | |
| occurrences (all) | 102 | 73 | |
| Chills | | | |
| subjects affected / exposed | 22 / 283 (7.77%) | 9 / 281 (3.20%) | |
| occurrences (all) | 26 | 11 | |
| Influenza like illness | | | |
| subjects affected / exposed | 27 / 283 (9.54%) | 20 / 281 (7.12%) | |
| occurrences (all) | 49 | 22 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 18 / 283 (6.36%) | 5 / 281 (1.78%) | |
| occurrences (all) | 21 | 6 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 72 / 283 (25.44%) | 50 / 281 (17.79%) | |
| occurrences (all) | 115 | 99 | |
| Pyrexia | | | |
| subjects affected / exposed | 71 / 283 (25.09%) | 40 / 281 (14.23%) | |
| occurrences (all) | 123 | 56 | |
| Fatigue | | | |
| subjects affected / exposed | 119 / 283 (42.05%) | 87 / 281 (30.96%) | |
| occurrences (all) | 247 | 158 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dysphonia | | | |
| subjects affected / exposed | 18 / 283 (6.36%) | 9 / 281 (3.20%) | |
| occurrences (all) | 18 | 9 | |
| Cough | | | |

| | | | |
|-----------------------------|--------------------|-------------------|--|
| subjects affected / exposed | 107 / 283 (37.81%) | 43 / 281 (15.30%) | |
| occurrences (all) | 211 | 74 | |
| Dyspnoea | | | |
| subjects affected / exposed | 65 / 283 (22.97%) | 39 / 281 (13.88%) | |
| occurrences (all) | 107 | 59 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 21 / 283 (7.42%) | 11 / 281 (3.91%) | |
| occurrences (all) | 30 | 14 | |
| Epistaxis | | | |
| subjects affected / exposed | 11 / 283 (3.89%) | 15 / 281 (5.34%) | |
| occurrences (all) | 13 | 18 | |
| Nasal congestion | | | |
| subjects affected / exposed | 23 / 283 (8.13%) | 7 / 281 (2.49%) | |
| occurrences (all) | 31 | 9 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 23 / 283 (8.13%) | 17 / 281 (6.05%) | |
| occurrences (all) | 25 | 21 | |
| Productive cough | | | |
| subjects affected / exposed | 26 / 283 (9.19%) | 11 / 281 (3.91%) | |
| occurrences (all) | 46 | 12 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 18 / 283 (6.36%) | 8 / 281 (2.85%) | |
| occurrences (all) | 25 | 12 | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 21 / 283 (7.42%) | 4 / 281 (1.42%) | |
| occurrences (all) | 27 | 4 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 25 / 283 (8.83%) | 13 / 281 (4.63%) | |
| occurrences (all) | 30 | 17 | |
| Depression | | | |
| subjects affected / exposed | 29 / 283 (10.25%) | 9 / 281 (3.20%) | |
| occurrences (all) | 35 | 10 | |
| Insomnia | | | |
| subjects affected / exposed | 80 / 283 (28.27%) | 65 / 281 (23.13%) | |
| occurrences (all) | 118 | 91 | |

| | | | |
|--|-------------------------|------------------------|--|
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 19 / 283 (6.71%) 36 | 14 / 281 (4.98%) 34 | |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 16 / 283 (5.65%) 36 | 17 / 281 (6.05%) 25 | |
| Weight decreased subjects affected / exposed occurrences (all) | 31 / 283 (10.95%) 40 | 13 / 281 (4.63%) 17 | |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 25 / 283 (8.83%) 37 | 12 / 281 (4.27%) 15 | |
| Fall subjects affected / exposed occurrences (all) | 24 / 283 (8.48%) 40 | 12 / 281 (4.27%) 21 | |
| Cardiac disorders | | | |
| Tachycardia subjects affected / exposed occurrences (all) | 16 / 283 (5.65%) 18 | 2 / 281 (0.71%) 2 | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 17 / 283 (6.01%) 21 | 9 / 281 (3.20%) 11 | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 56 / 283 (19.79%) 80 | 23 / 281 (8.19%) 28 | |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 18 / 283 (6.36%) 25 | 9 / 281 (3.20%) 17 | |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 25 / 283 (8.83%) 38 | 18 / 281 (6.41%) 25 | |
| Paraesthesia | | | |

| | | | |
|---|----------------------------|---------------------------|--|
| subjects affected / exposed occurrences (all) | 17 / 283 (6.01%) 24 | 12 / 281 (4.27%) 22 | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 40 / 283 (14.13%) 64 | 27 / 281 (9.61%) 43 | |
| Tremor subjects affected / exposed occurrences (all) | 28 / 283 (9.89%) 35 | 26 / 281 (9.25%) 29 | |
| Dizziness subjects affected / exposed occurrences (all) | 35 / 283 (12.37%) 46 | 30 / 281 (10.68%) 39 | |
| Blood and lymphatic system disorders | | | |
| Leukopenia subjects affected / exposed occurrences (all) | 29 / 283 (10.25%) 208 | 23 / 281 (8.19%) 89 | |
| Anaemia subjects affected / exposed occurrences (all) | 118 / 283 (41.70%) 343 | 117 / 281 (41.64%) 294 | |
| Neutropenia subjects affected / exposed occurrences (all) | 185 / 283 (65.37%) 1035 | 136 / 281 (48.40%) 592 | |
| Lymphopenia subjects affected / exposed occurrences (all) | 20 / 283 (7.07%) 91 | 17 / 281 (6.05%) 111 | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 92 / 283 (32.51%) 372 | 90 / 281 (32.03%) 339 | |
| Eye disorders | | | |
| Vision blurred subjects affected / exposed occurrences (all) | 28 / 283 (9.89%) 30 | 17 / 281 (6.05%) 18 | |
| Cataract subjects affected / exposed occurrences (all) | 59 / 283 (20.85%) 71 | 35 / 281 (12.46%) 41 | |
| Gastrointestinal disorders | | | |

| | | | |
|--|--------------------|--------------------|--|
| Abdominal pain | | | |
| subjects affected / exposed | 30 / 283 (10.60%) | 16 / 281 (5.69%) | |
| occurrences (all) | 38 | 24 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 29 / 283 (10.25%) | 13 / 281 (4.63%) | |
| occurrences (all) | 42 | 16 | |
| Constipation | | | |
| subjects affected / exposed | 94 / 283 (33.22%) | 77 / 281 (27.40%) | |
| occurrences (all) | 151 | 115 | |
| Diarrhoea | | | |
| subjects affected / exposed | 169 / 283 (59.72%) | 105 / 281 (37.37%) | |
| occurrences (all) | 474 | 216 | |
| Dyspepsia | | | |
| subjects affected / exposed | 29 / 283 (10.25%) | 9 / 281 (3.20%) | |
| occurrences (all) | 33 | 11 | |
| Nausea | | | |
| subjects affected / exposed | 86 / 283 (30.39%) | 53 / 281 (18.86%) | |
| occurrences (all) | 146 | 67 | |
| Stomatitis | | | |
| subjects affected / exposed | 19 / 283 (6.71%) | 6 / 281 (2.14%) | |
| occurrences (all) | 25 | 7 | |
| Toothache | | | |
| subjects affected / exposed | 17 / 283 (6.01%) | 10 / 281 (3.56%) | |
| occurrences (all) | 22 | 11 | |
| Vomiting | | | |
| subjects affected / exposed | 65 / 283 (22.97%) | 19 / 281 (6.76%) | |
| occurrences (all) | 99 | 26 | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 25 / 283 (8.83%) | 10 / 281 (3.56%) | |
| occurrences (all) | 32 | 13 | |
| Pruritus | | | |
| subjects affected / exposed | 34 / 283 (12.01%) | 31 / 281 (11.03%) | |
| occurrences (all) | 42 | 34 | |
| Rash | | | |

| | | | |
|---|--------------------------|--------------------------|--|
| subjects affected / exposed occurrences (all) | 51 / 283 (18.02%) 65 | 36 / 281 (12.81%) 48 | |
| Renal and urinary disorders Renal impairment subjects affected / exposed occurrences (all) | 33 / 283 (11.66%) 49 | 15 / 281 (5.34%) 17 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 75 / 283 (26.50%) 133 | 55 / 281 (19.57%) 85 | |
| Back pain subjects affected / exposed occurrences (all) | 76 / 283 (26.86%) 124 | 56 / 281 (19.93%) 86 | |
| Bone pain subjects affected / exposed occurrences (all) | 29 / 283 (10.25%) 37 | 16 / 281 (5.69%) 18 | |
| Muscle spasms subjects affected / exposed occurrences (all) | 87 / 283 (30.74%) 128 | 61 / 281 (21.71%) 106 | |
| Myalgia subjects affected / exposed occurrences (all) | 22 / 283 (7.77%) 25 | 17 / 281 (6.05%) 25 | |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 32 / 283 (11.31%) 38 | 24 / 281 (8.54%) 26 | |
| Muscular weakness subjects affected / exposed occurrences (all) | 29 / 283 (10.25%) 49 | 26 / 281 (9.25%) 35 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 47 / 283 (16.61%) 64 | 42 / 281 (14.95%) 56 | |
| Neck pain subjects affected / exposed occurrences (all) | 22 / 283 (7.77%) 28 | 13 / 281 (4.63%) 16 | |
| Infections and infestations | | | |

| | | |
|-----------------------------------|--------------------|-------------------|
| Urinary tract infection | | |
| subjects affected / exposed | 30 / 283 (10.60%) | 26 / 281 (9.25%) |
| occurrences (all) | 62 | 37 |
| Bronchitis | | |
| subjects affected / exposed | 60 / 283 (21.20%) | 45 / 281 (16.01%) |
| occurrences (all) | 112 | 66 |
| Conjunctivitis | | |
| subjects affected / exposed | 19 / 283 (6.71%) | 6 / 281 (2.14%) |
| occurrences (all) | 22 | 8 |
| Gastroenteritis | | |
| subjects affected / exposed | 25 / 283 (8.83%) | 9 / 281 (3.20%) |
| occurrences (all) | 35 | 9 |
| Influenza | | |
| subjects affected / exposed | 34 / 283 (12.01%) | 17 / 281 (6.05%) |
| occurrences (all) | 38 | 19 |
| Lower respiratory tract infection | | |
| subjects affected / exposed | 22 / 283 (7.77%) | 12 / 281 (4.27%) |
| occurrences (all) | 49 | 24 |
| Nasopharyngitis | | |
| subjects affected / exposed | 100 / 283 (35.34%) | 62 / 281 (22.06%) |
| occurrences (all) | 279 | 118 |
| Pneumonia | | |
| subjects affected / exposed | 51 / 283 (18.02%) | 27 / 281 (9.61%) |
| occurrences (all) | 80 | 34 |
| Respiratory tract infection | | |
| subjects affected / exposed | 38 / 283 (13.43%) | 29 / 281 (10.32%) |
| occurrences (all) | 73 | 49 |
| Rhinitis | | |
| subjects affected / exposed | 23 / 283 (8.13%) | 5 / 281 (1.78%) |
| occurrences (all) | 37 | 7 |
| Sinusitis | | |
| subjects affected / exposed | 27 / 283 (9.54%) | 13 / 281 (4.63%) |
| occurrences (all) | 42 | 19 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 123 / 283 (43.46%) | 74 / 281 (26.33%) |
| occurrences (all) | 330 | 147 |

| | | | |
|------------------------------------|-------------------|-------------------|--|
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 50 / 283 (17.67%) | 36 / 281 (12.81%) | |
| occurrences (all) | 81 | 50 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 34 / 283 (12.01%) | 22 / 281 (7.83%) | |
| occurrences (all) | 78 | 35 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 24 / 283 (8.48%) | 16 / 281 (5.69%) | |
| occurrences (all) | 46 | 20 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 58 / 283 (20.49%) | 35 / 281 (12.46%) | |
| occurrences (all) | 118 | 77 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 18 / 283 (6.36%) | 17 / 281 (6.05%) | |
| occurrences (all) | 26 | 22 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 22 / 283 (7.77%) | 14 / 281 (4.98%) | |
| occurrences (all) | 68 | 24 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 16 June 2014 | The overall reason for this amendment was 1) The sample size was changed to reflect the median progression-free survival (PFS) assumption for the comparator arm; 2) Lenalidomide global pregnancy prevention plan was added; Feedback from investigators and health authorities was incorporated. |
| 20 November 2014 | The overall reason for this amendment was 1) The requirements for bone marrow sample collection were modified to allow for differences across countries in local clinical practice; 2) Other protocol procedures were clarified based on feedback from investigative sites; 3) Changes from France (FRA)-1 and Japan (JPN)-1 amendments were rolled into the global interim (INT)-2 amendment. |
| 26 May 2016 | The overall reason for the amendment was to include that following the positive interim analysis of efficacy results, subjects who were randomized to the Rd group and who had sponsor-confirmed disease progression were offered treatment with daratumumab monotherapy. Subjects who received daratumumab monotherapy had a limited schedule of assessments and limited adverse event (AE) collection. |
| 01 November 2016 | The overall reason for the amendment was to include additional time points for collection of bone marrow aspirate, for purposes of minimal residual disease (MRD) assessment, to align with newly defined categories of MRD-negativity. |
| 22 January 2018 | The overall reason for the amendment was to allow disease evaluations to be performed by the central laboratory on the current schedule until median PFS was reached in the daratumumab, lenalidomide, and low-dose dexamethasone (DRd) arm of the randomized portion of the study, for uniformity in data analysis. Thereafter, disease evaluations for all subjects were performed by local laboratories according to each site's standard of care. In addition, patient reported outcome (PRO) assessments were collected for an extended duration intended to ensure optimal evaluation of long-term health-related quality of life parameters. |
| 05 December 2018 | The overall reason for the amendment was to include changes in response to identification of a new important risk (Hepatitis B Virus reactivation). |
| 12 June 2019 | The overall reason for the amendment was to align guidance on monitoring and management of Hepatitis B Virus reactivation with other daratumumab studies. |
| 09 April 2020 | The overall reason for the amendment was to include changes to provide flexibility for study investigators to prioritize the safety of their patients during the global COVID-19 pandemic. To ensure continuity of study treatment, while limiting subjects' time spent at the study center, subjects who were receiving daratumumab intravenous (16 milligrams per kilogram [mg/kg]) were given the option to switch to daratumumab subcutaneous (SC) (1800 mg) on Day 1 of any cycle, at the discretion of the investigator. Assessments to evaluate the immunogenicity of recombinant human hyaluronidase PH20 (rHuPH20) were added as part of this protocol amendment. |
| 06 April 2021 | The overall reason for the amendment was to clarify that sites would be notified of the clinical cutoff (CCO) for the final overall survival (OS) analysis, to define the end of the electronic case report form (eCRF) data collection, to amend the end of study, and to clarify that subjects who were benefiting from study treatment would be able to continue to receive study treatment from the final OS analysis until the end of study when alternative access to daratumumab was not available. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported